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EXAMINER
KUBELIK, ANNE R

ART UNIT	PAPER NUMBER
1638	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/633,274	Applicant(s) PENTAL ET AL.	
	Examiner Anne Kubelik	Art Unit 1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 August 2000*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4)☐ Interview Summary (PTO-413) Paper No(s). _____.
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other:

DETAILED ACTION

1. Claims 1-28 are pending.

2. The drawings are objected to for the reasons indicated on accompanying form PTO 948. Correction is required.

3. Applicant has not complied with the requirements of 37 CFR 1.63(c), since the oath or declaration does not acknowledge the filing of any foreign application. A new oath or declaration is required in the body of which the present application should be identified by application number and filing date.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-28 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for insulator sequences that do not comprise enhancers or other types of transcriptional regulatory elements that can act on the lethal gene transcriptional unit, does not reasonably provide enablement for insulator sequences that do comprise enhancers or other types of transcriptional regulatory elements that can act on the lethal gene transcriptional unit. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are broadly drawn to an insulator construct that uses an insulator sequence to separate a lethal gene transcriptional unit from a selectable marker transcriptional unit. The instant specification, however, fails to provide guidance for the sequence of this insulator sequence.

Not all "insulator" sequences will prevent undesired transcription of a lethal gene construct. If the "insulator" sequence contains an enhancer or promoters transcription of a construct can unexpectedly be enhanced. Similarly, if the "insulator" sequence contains a negative regulatory element, transcription of a gene can be inhibited. For example, the 5' flanking region of the *Cucumis* NADH-dependent hydroxypyruvate reductase gene was found to contain a negative regulatory element, and the 3' region was found to enhance expression of minimal promoter (Daniel et al, 1995, Plant Mol. Biol. 28:821-836, pg 834).

Additionally, lethal genes whose transcription is targeted to specific tissues like roots are not likely to produce living male-sterile plants. Thus, constructs in which the lethal gene is operably linked to any tissue-specific promoter cannot be used to make male-sterile plants.

Given the claim breath, unpredictability, and lack of guidance as discussed above, undue experimentation would have been required by one skilled in the art to develop and evaluate an insulator construct that uses an insulator sequence to separate a lethal gene transcriptional unit from a selectable marker transcriptional unit and methods for its use.

6. Claims 1-28 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The only enabled insulator sequence is the one of the plasmid in Fig. 1. Thus, the

invention appears to employ novel plasmids contained in microorganisms. Since the plasmid contained in the microorganism is essential to the claimed invention, it must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. If the plasmid contained in the microorganism is not so obtainable or available, the requirements of 35 USC 112 may be satisfied by a deposit of the microorganism. The specification does not disclose a repeatable process to obtain the plasmid contained in the microorganism and it is not apparent if the plasmid is readily available to the public. Thus, a deposit is required for enablement purposes.

If the deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicant, or a statement by an attorney of record over his or her signature and registration number, stating that the specific strain has been deposited under the Budapest Treaty and that the strain will be irrevocably and without restriction or condition released to the public upon the issuance of a patent, would satisfy the deposit requirement made herein.

If the deposit has not been made under the Budapest Treaty, then in order to certify that the deposit meets the criteria set forth in 37 C.F.R. 1.801-1.809, Applicant may provide assurance of compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that

(a) during the pendency of this application, access to the invention will be afforded to the Commissioner upon request;
(b) all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;
(c) the deposit will be maintained in a public depository for a period of 30 years or 5 years after the last request or for the enforceable life of the patent, whichever is longer;
(d) a test of the viability of the biological material at the time of deposit (see 37 CFR 1.807); and,
(e) the deposit will be replaced if it should ever become inviable.

7. Claims 1-28 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to a multitude of DNA molecules that act as insulator constructs. The specification does not describe the coding sequence of the insulator sequence within these constructs, nor those of the lethal gene or selectable marker within the construct.

No description is provided as to the structural features that distinguish insulator constructs from other DNA sequences or other genomic plant sequences.

Hence, Applicant has not, in fact, described insulator constructs and insulator sequences within the full scope of the claims, and the specification fails to provide an adequate written description of the claimed invention.

Therefore, given the lack of written description in the specification with regard to the structural and physical characteristics of the claimed compositions, and given the high level of unpredictability in this art, one skilled in the art would not have been in possession of the genus claimed at the time this application was filed.

See *University of California v. Eli Lilly*, 119 F.3d 1559, 43 USPQ 2d 1398 (Fed, Cir. 1997):

> The name cDNA is not in itself a written description of that DNA; it conveys no distinguishing information concerning its identity. While the example provides a process for obtaining human insulin-encoding cDNA, there is no further information in the patent pertaining to that cDNA's relevant structural or physical characteristics; in other words, it thus does not describe human insulin cDNA .... Accordingly, the specification does not provide a written description of the invention ....

and at pg 1406:

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicted, does not suffice to define the genus because it is only an indication of what the genes does, not what it is.

See *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ 2d 1016 at page 1021:

> A gene is a chemical compound, albeit a complex one, and ... conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials .... Conception does not occur unless one has a mental picture of the structure of the chemical or is able to define it by

> its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it. It is not sufficient to define it solely by it principal biological property, *e.g.*, encoding human erythropoietin, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 1-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Dependent claims are included in all rejections.

Claim 1 is indefinite in the recitation of the word "including" in parts i) and ii) and claim 16 for its recitation of the word in parts i)a), and i)b). It is unclear if this word is intended to be open or closed. If open language is intended, the word should be replaced with --comprising--.

Claims 1 and 16 are indefinite for their recitation of "Insulator sequence" and Insulator DNA sequence", respectively. The size and nature of this sequence is unclear. For purposes of examination, sequences were assumed to be of any length. Such treatment does not relieve Applicant of the responsibility to respond to this rejection.

Claim 3 is indefinite because all members of the group are not written in the same format. The word --gene-- should be inserted after each of "*barnase*", "*RNaseT1*", "*binase*", "*rolB*", and "*rolC*". Additionally, "chain-coding" should be deleted.

Similarly, the word --gene-- should be inserted after "*barnase*" in claims 4 and 17.

Claims 4 and 17 recite the limitation "the preferred lethal gene" in line 4. There is insufficient antecedent basis for this limitation in the claims.

Claims 6 and 18 recite the limitation "the preferred tissue specific promoter" in line 1. There is insufficient antecedent basis for this limitation in the claims.

Claims 7 and 27 recite the limitation "the marker gene" in lines 1 and 2, respectively. There is insufficient antecedent basis for this limitation in the claims.

Claims 8 and 19 recite the limitation "the preferred marker gene" in line 1. There is insufficient antecedent basis for this limitation in the claims.

Claim 9 recites the limitation "the strong constitutive promoter for expression of the *bar* gene" in lines 1-2. There is insufficient antecedent basis for both the limitation "the strong constitutive promoter for expression..." and "the *bar* gene" in the claim.

Claim 10 is indefinite in its recitation of "sequence derived from genomic DNA of a plant". The size of this sequence is not clear. For purposes of examination, a sequence as small as one base was assumed. Such treatment does not relieve Applicant of the responsibility to respond to this rejection.

Claims 12 and 21 recite the limitation "the preferred length" in line 1. There is insufficient antecedent basis for this limitation in the claims.

Claim 13 is not written in proper Markush format. The plants and plant parts should recited in the alternative; thus, "and" in line 1 should be replaced with --or--. See MPEP § 2173.05(h).

Claim 15 recites the limitation "The preferred plant" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 20 recites the limitation "the preferred constitutive promoter" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 26 recites the limitation "the above male sterile plants" in lines 1-2. There is insufficient antecedent basis for this limitation in the claim.

Regarding claim 23, the word "preferably" renders the claim indefinite because it is unclear whether the limitation(s) following the word are part of the claimed invention. See MPEP § 2173.05(d).

Regarding claims 4, 6, 8, 12, 15 and 17-21, the word "preferred" renders the claim indefinite because it is unclear whether the limitations following the word are part of the claimed invention. See MPEP § 2173.05(d).

Claims 3, 5, 7 and 14 not written in proper Markush format. The claims should be in the format "selected from the group consisting of A, B, C and D." In claims 3, 5 and 7 "the group comprising" should be replaced with -- the group consisting of--. In claim 14, "the group of" should be replaced with --the group consisting of-- and "dicotyledonous or monocotyledonous plants" should be replaced with -- a dicotyledonous plant and a monocotyledonous plant--. See MPEP § 2173.05(h).

In claims 15 and 22 the phrase "a dicotyledonous plant *Brassica juncea*" is unduly wordy and awkward. It is suggested that the phrase be replaced with --*Brassica juncea*--.

Claim 15 is written in the incorrect format. The claim should not be written as a complete sentence. Thus, the claim should be --The plant of claim 13, where the plant is *Brassica juncea*.--

Claim 16 is indefinite for its recitation of "tissue specific promoter end" in part i)a). It is unclear what a promoter end is, and if it is a portion of a promoter, the size of that portion.

The steps of the method of claim 16 should be written in gerund form. Thus, "identification of" in step iii) should be --identifying--.

It is unclear, in claim 16, step iii) what morphological observations identify a plant as male sterile, particularly as step iv) requires plants with normal vegetative morphology.

Claim 16 is indefinite in the recitation of the word "including" in parts i)a) and b) and claim 1 in parts i) and ii). It is unclear if this word is intended to be open or closed. If open language is intended, the word should be replaced with --comprising--.

Claim 23 recites the limitation "*Brassica juncea*" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 26 recites the limitation "the T-DNA insert" in lines 2-3. There is insufficient antecedent basis for this limitation in the claim.

Claim 28 recites the limitation "the T1 plants" in line 1. There is insufficient antecedent basis for this limitation in the claim. Additionally, there is no antecedent basis for "selected backcrossed progeny" in lines 1-2, as no backcrossed progeny were selected in the method of claim 16.

It is unclear where in the method of claim 16 the backcrossing and testing steps of claim 24 are performed. The method of claim 16 already has a backcrossing step.

It is unclear where in the method of claim 16 the Southern hybridization step of claim 25 is performed.

It is unclear in the method of claim 27 how transferring seeds on selective media would test for segregation of a marker gene. A step appears to be missing.

10. Claims 16-28 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. Method steps must be circular; the final step must generate the item the method is intended to produce. For example, the method of obtaining male sterile plants in claim 16 ends in obtaining stable transfer of a male sterile phenotype, when it should end in the production male sterile plants.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

12. Claims 1-4, 7-10, 13-14, 16-17, 19-20, 24 and 26-28 are rejected under 35 U.S.C. 102(e) as being anticipated by Williams et al (US Patent 5,977,433, filed June, 1992).

Williams et al teach constructs comprising the *barnase* gene operably linked to the pollen-specific Zm13 promoter, the *neo* or *bar* gene operably linked to the 35S3 constitutive promoter, wherein the two genes are separated by a "insulator sequence" that is about 1200 nucleotides long and that encodes the barstar gene operably linked to the TA29 promoter (column 14, line 40, to column 15, line 49, SEQ ID NOs:2, 3 and 17). This "insulator" sequence

would comprise at least one base derived from genomic DNA; additionally, the TA29 promoter is derived from plant genomic DNA. Williams et al also teach male-sterile maize plants transformed with these constructs and analyzed by Southern hybridization and testcrosses (column 18, line 24, to column 20, line 24).

13. Claims 1-4, 7-9 and 13-14 are rejected under 35 U.S.C. 102(b) as being anticipated by Chang et al (1997, US Patent 5,610,042).

Chang et al teach constructs comprising the *barnase* gene operably linked to the stamen-specific rice E1 promoter, the *bar* gene operably linked to the 35S constitutive promoter, wherein the two genes are separated by a "insulator sequence" that is about 23 nucleotides long (SEQ ID NOs:1 and 3). Chang et al also teach male-sterile rice, maize plants and *Brassica napus* transformed with these constructs and their progeny (column 15, line 13, to column 18, line 66).

Claim Rejections - 35 USC § 103

14. The following is a quotation of 35 U.S.C. 103(a), which forms the basis for all obviousness rejections set forth in this Office action

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

15. Claims 1-14, 16-21 and 24-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Williams et al (*supra*) in view of Mariani et al (1997, US Patent 5,689,041).

The claims are drawn to a construct comprising a lethal gene transcription unit and a selectable marker gene transcription unit, wherein the two transcription units are separated by a "insulator" sequence of unspecified composition and wherein the lethal gene transcription unit

has a tissue-specific promoter. The claims are also drawn to male-sterile plants comprising the construct and a method of using the construct to obtain male-sterile plants.

Williams et al teach constructs comprising the *barnase* gene operably linked to the pollen-specific Zm13 promoter, the *neo* or *bar* gene operably linked to the 35S3 constitutive promoter, wherein the two genes are separated by a "insulator sequence" (column 14, line 40, to column 15, line 49, SEQ ID NOs:2, 3 and 17). Williams et al also teach male-sterile maize plants transformed with these constructs and analyzed by Southern hybridization and testcrosses (column 18, line 24, to column 20, line 24). Williams et al do not disclose insulator sequences of at least 2 or 5 kb or that are derived from genomic plant DNA, nor do they disclose methods of transformation of *Brassica juncea*.

Mariani et al teach constructs in which the barnase gene is operably linked to the anther-specific TA29 promoter and a variety of monocots and dicots transformed with this construct (claims 37 and 46).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to produce male-sterile plants using the constructs taught by Williams et al, and to modify that to use in those constructs the promoter described in Mariani et al. One of ordinary skill in the art would have been motivated to do so because selection of tissue-specific promoter is an obvious design choice, as is the length of the region of DNA separating transcription units.

16. Claims 15 and 22-23 rejected under 35 U.S.C. 103(a) as being unpatentable over Williams et al in view of Mariani et al as applied to claims 1-14, 16-21 and 24-28 above, and further in view of Mathews et al (1990, Plant Sci. 72:245-252).

The claims are drawn to a construct comprising a lethal gene transcription unit and a selectable marker gene transcription unit, wherein the two transcription units are separated by a "insulator" sequence of unspecified composition and wherein the lethal gene transcription unit has a tissue-specific promoter. The claims are also drawn to male-sterile *Brassica juncea* plants comprising the construct and a method of using the construct to obtain male-sterile *Brassica juncea* plants.

Williams et al in view of Mariani et al disclose constructs comprising the *barnase* gene operably linked to the pollen-specific TA29 promoter, the neo or bar gene operably linked to the 35S3 constitutive promoter, wherein the two genes are separated by a "insulator sequence" that is about 1200 nucleotides long. Williams et al in view of Mariani et al also teach a variety of monocots and dicots male-sterile plants transformed with these constructs and analyzed by Southern hybridization and testcrosses (column 18, line 24, to column 20, line 24). Williams et al in view of Mariani et al do not disclose male-sterile *Brassica juncea* transformed with these constructs.

Mathews et al teach a method of *Agrobacterium*-mediated transformation of *Brassica juncea*.

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to produce male-sterile plants using the lethal gene constructs taught by Williams et al in view of Mariani et al, and to modify that to transform *Brassica juncea*. as described in Mathews et al. One of ordinary skill in the art would have been motivated to do so because of the economic importance of mustard plants and the desirability of using male sterility systems in developing new varieties.

Conclusion

17. No claim is allowed.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (703) 308-5059. The examiner can normally be reached on Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Paula K. Hutzell, can be reached on (703) 308-4310. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Anne R. Kubelik, Ph.D.
October 31, 2001

DAVID T. FOX
PRIMARY EXAMINER
GROUP ~~180~~ 1638